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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/587,790	07/28/2006	Paul Bamborough	PB60706	2091

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EXAMINER	
PAGONAKIS, ANNA	
ART UNIT	PAPER NUMBER
1614	

NOTIFICATION DATE	DELIVERY MODE
07/15/2009	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/587,790	BAMBOROUGH ET AL.	
	Examiner	Art Unit	
	ANNA PAGONAKIS	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 April 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-13 and 18-23* is/are pending in the application.

4a) Of the above claim(s) *18 and 23* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-13 and 19-22* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *10/23/2008, 5 sheets*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's amendment filed 4/4/2009 has been received and entered into the present application.

Claims 1-13 and 18-23 are pending. Accordingly, claims 18 and 23 remain withdrawn.

The information disclosure statement of 1/7/2009 has been considered and is attached. Further, the traversal of the Lack of Unity requirement has been addressed in the Office Action mailed on 1/7/2009.

Applicant's arguments, filed 4/4/2009 have been fully considered. Rejections not reiterated from previous Office Actions are hereby withdrawn. The following rejections are either reiterated or newly applied. They constitute the complete set of rejections presently being applied to the instant application.

Claim Rejections - 35 USC § 112, First Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-13 and 19-22 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

In this regard, the application disclosure and claims have been compared per the factors indicated in the decision *In re Wands*, 8 USPQ 2d 1400 (Fed. Cir., 1988) as to undue experimentation. The factors include:

1) the nature of the invention;

2) the breadth of the claims;

3) the predictability or unpredictability of the art;

4) the amount of direction or guidance presented;

5) the presence or absence of working examples;

6) the quantity of experimentation necessary;

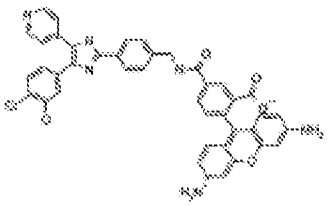
7) the state of the prior art; and,

8) the relative skill of those skilled in the art.

The relevant factors are addressed below on the basis of comparison of the disclosure, the claims and the state of the prior art in the assessment of undue experimentation.

The instant claims are directed to the compounds of formula I to be used for the treatment of various conditions associated with p38 kinase inhibition. However, the instant specification as originally filed lacks adequate guidance, direction or discussion to apprise the skilled artisan how the claimed compounds may be used to achieve the disclosed utilities for treating conditions wherein p38 kinase inhibition has been implicated and particularly how it is implicated in the treatment of cancer, with at least a reasonable expectation of successfully achieving the treatment of the same. The instant specification fails to present any evidence, either in the form of data or scientifically sound reasoning, which would provide such a reasonable expectation that the claimed compounds would have been effective to treat the disclosed disorders. Though it is noted that Applicant need not necessarily demonstrate the precise manner in which the claimed therapeutic agent(s) ameliorate a particular disease state, such a mechanism must be elucidated in cases where Applicant relies upon a correlation between the particular activity of a compound and a reasonable expectation of efficacy in treating a particular disease.

In the instant case, Applicant relies upon the experimental protocols found on pages 108-110 of the instant specification. It is noted that the experimental protocols only mention the following compound:



and details a procedure of how to measure p38 kinase inhibition and how to determine whether cell proliferation has been halted. Neither p38 kinase inhibition nor cessation of cell proliferation with the instantly claimed compounds has been demonstrated. Further, Applicant relies on the underlying the purported biological activity to establish that the genus of compounds instantly claimed would have been useful for treating conditions in which p38 kinase inhibition "is implicated". Notably, however, the purported effect and/or specific interaction of the instantly claimed compound with p38 kinase inhibition and treatment of diseases associated thereof is never described within the four corners of the instant specification. In other words, though Applicant's inventive concept rests upon the correlation between the particular activity of the claimed compounds in p38 kinase inhibition to provide a reasonable expectation of efficacy in treating the disclosed disease(s) or disorder(s), the actual activity of the instantly claimed compound and the receptor with which it is proposed to interact is not adequately described in the accompanying specification so as to enable the full scope of the instant claims.

Applicant provides for the synthesis of the instantly claimed compounds of formula I, as well as exemplary pharmaceutical formulations that comprise an active ingredient of the claimed compounds of the invention. Though Applicant's examples in this regard are duly noted, Applicant has failed to demonstrate that the instantly claimed compounds of formula I actually functions to achieve the disclosed therapeutic use of treating conditions associated with p38 kinase inhibition, such that one of skill in the art would have thereby recognized its efficacious use in treating any one or more of the disclosed disease states. The specification fails to present either view a working or prophetic example(s) or a clear, scientifically sound explanation as to what, in fact, enables treating conditions associated with p38 kinase inhibition, such that the

skilled artisan would have been imbued with at least a reasonable expectation of predictability of action in using the instantly claimed compound for use in treating any one or more of the disorders disclosed as being responsive to such an effect. Absent such guidance, the experimentation required to determine if there is any activity of any of the compounds in treating conditions associated with p38 kinase inhibition, and further, to determine, without needing to resort to random speculation, what therapeutic amounts would be available to even start testing for a therapeutic effect, would clearly be undue. Further, it is noted that, while the lack of a working embodiment cannot be the *sole* factor in determining enablement, the absence of substantial evidence commensurate in scope with the breadth of the presently claimed subject matter, in light of the unpredictable nature of the chemical and pharmaceutical arts and the limited direction that Applicant has presented, provides additional weight to the present conclusion of insufficient enablement in consideration of the *Wands* factors as a whole.

Although the instant specification states that the instantly claimed genus of compounds, which encompasses the compounds of formula I, interact in some (unspecified) manner conditions, specifically cancer, where p38 kinase inhibition "is implicated", the disclosure fails to provide any mechanistic discussion or provide any evidence or data, preclinical or otherwise, supporting the concept that the instantly claimed compound would, in fact, be effective to treat conditions associated with p38 kinase inhibition, so as to achieve the therapeutic treatment of the disclosed disorders, specifically cell proliferation. In the absence of such discussion or evidence, it is clear that the instant specification fails to support the enablement of the instantly claimed compounds in treating conditions associated with p38 kinase inhibition, specifically cell proliferation, such that the skilled artisan would have reasonably expected that the instantly claimed compound, effective in this manner, would have functioned to achieve the disclosed utility.

As stated in MPEP §2164.04[R-1], "Doubt may arise about enablement because

information is missing about one or more essential parts or relationships between parts which one skilled in the art could not develop without undue experimentation." In the instant case, the information that is missing is a clear correlation between the claimed compound and its efficacy in treating the disclosed conditions, either through specific evidence in the form of data demonstrating such a fact or at least a sound mechanistic correlation between the claimed compound, *its ability to function in such a manner* and the amenability of the claimed disease state to treatment using an agent capable of functioning in this manner. Though one of skill in the art might very well known how to treat a patient with the claimed compound once a diagnosis had been made of the disorder (e.g., cell proliferation, etc.), it remains that the instant specification conspicuously fails to provide any guidance or direction in support of the *reasonable expectation of success* in actually effecting the treatment of the disclosed disorders using the instantly claimed compound in the absence of any evidence supporting the allegation that the claimed compound is, in fact, effective to achieve such a therapeutic objective, either by reduction to practice or at least by elucidating the mechanism by which the claimed compound works and correlating such activity to therapeutic improvement of the disclosed disorders or diseases. In the absence of this information, the specification fails to provide adequate guidance and/or direction to one of skill in the art at the time of the invention that would have enabled such a person to practice the instantly claimed invention without having to resort to undue experimentation to determine how, in fact, one would achieve the instantly disclosed therapeutic objective(s).

The basis for the present rejection is not simply that experimentation would be required, since it is clear from the state of the prior art and Applicant's disclosure and remarks that experimentation in this particular art is not at all uncommon, but that the experimentation required in order to practice the full scope of the invention would be *undue*. Please reference *In re Angstadt*, 537 F.2d 498, 504, 190 USPQ 214, 219 (CCPA 1976), which states, "The test of enablement is not whether any experimentation is necessary, but whether, *if experimentation is*

necessary, it is undue." (emphasis added) Accordingly, in the absence of any adequate disclosure, direction or guidance as to how one would go about using the instantly claimed compound with a reasonable expectation of successfully treating the disclosed disorder(s), it remains that the pharmaceutical, chemical and medical arts are notoriously complex such that methods of use would have been sufficiently unpredictable to warrant the need for undue experimentation to actually practice the full scope of the invention as instantly claimed.

In view of the discussion of each of the preceding seven factors, the level of skill in the art is high and is at least that of a medical doctor or scientist with several years of experience in the art.

As the cited art and discussion of the above factors establish, practicing the claimed method in the manner disclosed by Applicant would not imbue the skilled artisan with a reasonable expectation or ability to make and use the full scope of the invention as instantly claimed, given the disclosure and supporting examples provided in the present specification and the state of the art at the time of the invention. In order to actually achieve the claimed invention, it is clear from the discussion above that the skilled artisan could not rely upon Applicant's disclosure as required by 35 U.S.C. 112, first paragraph, and would have no alternative recourse but the impermissible burden of undue experimentation in order to practice the full scope of the embodiments presently claimed.

Remarks to Applicant's Response

Applicant alleges that the compound of page 5 of the Office Action is not a compound of formula I but rather a fluorescent ligand used in the assay. The Examiner agrees with Applicant. It is noted that the Examiner did not state that the compound was in fact a compound of formula I, but rather was reiterating that in fact the compound was used in the assay. *Applicant alleges that the assays used were art recognized assays for determining inhibitory activity of a compound*

against p38 kinase. This is not persuasive. Firstly, the assay simply leads to the conclusion that binding in fact occurs. The assay does not lead the conclusion that this binding is null, inhibitory or activating. Secondly, Applicant alleges that the assay is a well recognized assay for determine p38 kinase activity, but advances no specific evidence, aside from Counsels' own argument, in support of this position. This assertion by Counsel is an unsupported allegation and fails to take place of evidence in the record. Statements of this nature are clearly unpersuasive in accordance with the guidance provided at MPEP 2145, which states, "The arguments of counsel cannot take the place of evidence in the record. In re Schulze, 346 F.2d 600, 602 125 USPQ 716, 718 (CCPA 1965); In re Geisler, 116 F.3d 1465, 43 USPQ2d 1362 (Fed. Cir. 1997)." Accordingly, there is no reason or basis advanced by Applicant to reasonably assume that the fluorescence anisotropy kinase binding assay does in fact lead to the conclusion that p38 kinase inhibition occurs, and as a result, such an argument is unpersuasive in establishing nonobviousness of the claimed invention.

Conclusion

No claim is found to be allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to ANNA PAGONAKIS whose telephone number is (571)270-3505. The examiner can normally be reached on Monday thru Thursday, 9am to 5pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin H. Marschel can be reached on 571-272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

AP

/Patricia A. Duffy/
Primary Examiner, Art Unit 1645